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COOPER & DUNHAM, LLP
30 Rockefeller Plaza
20th Floor
NEW YORK, NY 10112

EXAMINER	
HAMA, JOANNE	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/632,581	RODRIGUEZ ET AL.	
	Examiner	Art Unit	
	JOANNE HAMA	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7,9-12,25-28,48 and 51-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7,9-12,25-28,48 and 51-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant filed a response to the Non-Final Action of September 2, 2009 on March 5, 2010.

No amendments to the claims were filed. As such, Applicant's response will apply to the claims filed July 7, 2009.

Claims 6, 8, 13-24, 29-47, 49, 50 are cancelled.

Claims 1-5, 7, 9-12, 25-28, 48, 51-54, drawn to isolated adult multipotent human stem cells, are under consideration.

Information Disclosure Statement

Applicant filed an Information Disclosure Statement (IDS) on March 5, 2010. The IDS has been considered.

Maintained Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 7, 9-12, 25-28, 48, 51-54 remain rejected in modified form under 35 U.S.C. 103(a) as being unpatentable over Katz et al., PCT Publication No. WO 00/53795, publication date, September 14, 2000, previously cited, Akanbi et al., 1994, J.

Anim. Sci., 72: 2828-2835, previously cited, Hedrick et al., US Patent Application US 2003/0082152, published May 1, 2003, previously cited, Haynesworth et al., US Patent 5,733,542, patented March 31, 1998, previously cited Tremain et al., 2001, Stem Cells, 19: 408-418, previously cited, Djian et al., 1983, J. Clin. Invest. 72: 1200-1208, previously cited, Young et al., US Patent Application Publication, US 2004/0033214, published February 19, 2004, Didinksy et al., 1981, Journal of Cellular Physiology, 109: 171-179, for reasons of record, June 25, 2008, January 26, 2009, September 2, 2009.

The rejection of June 25, 2008 and September 2, 2009 are reproduced below for Applicant's convenience. The Examiner addresses claim 25, step e) following the reiteration of the rejection at hand.

Katz et al. teach human lipo-derived stem cells (Katz et al., Example 1). Katz et al. teach that these stem cells can differentiate into adipocytes, osteocytes, myocytes, or chondrocytes (see table on page 18) and that the telomerase activity was similar to that exhibited by previously reported human stem cells (Katz et al., page 18, 1st parag.). Katz et al. also teach how to isolate the stem cells from adipose tissue. Adipose tissue is obtained from liposuction patients, rinsed with PBS, digested with collagenase, and spun twice in a centrifuge. Following the second spin, the cells were plated (Katz et al. Example 1).

While Katz et al. teach that the adipose tissue is obtained from liposuction (and implies the tissue is from adults), Katz et al. do not teach obtaining the tissue from children.

Akanbi et al. teach that adipose precursor cells from young animals replicate faster than cells from older animals and/or contain more clones capable of full differentiation into adipocytes (Akanbi et al., page 2828, 2nd col., 1st parag.).

It would have been obvious to one of ordinary skill in the art to obtain stem cells from adipose tissue of children using the teachings of Katz et al. and Akanbi et al. An artisan would have taken the method of obtaining stem cells from adipose tissue and carried out the procedure using adipose tissue from children since Akanbi et al. teach that cells obtained from young animals replicate faster and differentiate better than cells obtained from older animals.

It is noted that neither Katz et al. nor Akanbi et al. teach that stem cells obtained from adipose tissue of children have particular characteristics, such as those recited in claim 1. However, because the method of obtaining the stem cells from adipose tissue (Katz et al.) is the same as the claimed invention, the cells obtained from children would have these characteristics. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

With regard to the claims being drawn to cells obtained by selecting "CA" cells that have an adhesion rate of less than 12 hours (claim 25), it is routine in the art to plate cells overnight, allow them to adhere to the plate, and rinse them the next day in order to remove debris and residual non-adherent red blood cells (Hedrick et al., page 66, parag. 202). As such, Hedrick et al. teach that it is routine in the art that stem cells can be obtained following overnight plating of cells. With regard to claim 25 being drawn to "enriching the CA population" and "inducing proliferation of CA", Hedrick et al. teach that these plated cells can remain stem cells if they are maintained at sub-confluent levels (Hedrick et al., page 66, parag. 202). Hedrick et al.'s teaching is readable on the claims because Hedrick et al.'s population is enriched by the PBS washing and by keeping the cells confluent to maintain their multipotency.

Applicant amended the claims on July 7, 2009. The Examiner addressed these amendments as follows.

With regard to obtaining cells that adhered to the culture plate 12 hours after starting the culture (claim 25, steps c) and d)), the art teaches that stem cell lines originate from a single cell. To obtain these single cells, the art teaches that single cell-derived colonies can be isolated by using cloning cylinders and that the single cells can be tested for colony-forming efficiency, which is a predictor for life span and differentiation potential of the cell (Tremain et

al., page 409, 2nd col. under Isolation and Culture of Human MSCs). In addition to using a cloning ring to isolate a single cell, the art teaches that a period of 12 hours is sufficiently long to allow adherence of cells, but is too brief for appreciable replication (Djian et al., page 1201, 2nd col., 1st parag. under Primary culture and cloning of adipocyte precursors). As such, allowing cells to adhere for 12 hours maximizes the number of cells that adhere to the plate and minimizes any confusion that two cells sitting next together are two different cells that plated next to each other or is the result of cell division. As such, an artisan would plate cells for 12 hours.

To better address the limitations of claim 25, step e), wherein the cells are cultured for 50-80 population doublings and diluting the cells 2-3 fold at each transfer until a quiescent population of cells is obtained, at the time of filing, the art teaches that there is a relationship between population doublings and stem cells. Young et al. teach that while progenitor stem cells are capable of self-replication but have a limited life-span (approximately 50-70 cell doublings) before programmed cell senescence occurs (Young et al, page 6, parag. 0006), pluripotent cells, however, are lineage-uncommitted and are capable of extended self-renewal as long as they remain lineage-uncommitted. Given this teaching, an artisan would have subjected the cells obtained after 12 hours of allowing them to adhere and then subjected them to 50-70 doublings in order to eliminate those that were not pluirpotent stem cells. Those cells that were not pluripotent would have undergone senescence and would have been eliminated from the culture. With regard to the dilutions at which the cells are cultured, Didinsky et al. teach that it is routine to use dilutions of 1:2 or 1:3 to separate cells during population doubling studies (Didinksy et al., page 173, 1st col., 2nd parag.).

Applicant's arguments filed March 5, 2010 have been fully considered but they are not persuasive.

Applicant indicates that 7 documents were used to formulate the 103 rejection and that an artisan would not use a high number of documents in an obvious manner. (Applicant's response, page 2). In response to applicant's argument that the examiner has combined an excessive number of references, reliance on a large number of references in a rejection does not, without more, weigh against the obviousness of the claimed invention. See *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991).

Applicant indicates that with regard to steps c) and d) of claim 25, the Examiner cited Tremain et al. Applicant indicates that Tremain et al. is relative to the isolation of stem cells from bone marrow. As such, Tremain et al. do not teach the isolation from adipose tissue. Applicant refers to Exhibit E, Bernardo et al. who teach that bone marrow is rich in stem cells and fat tissue contains mainly differented cells (Applicant's emphasis, Applicant's response, page 3). In response, this is not persuasive. Applicant is correct that Tremain et al. does not teach isolation of stem cells from adipose tissue. Tremain is not used in a 102 rejection and is a 103 rejection wherein the teaching of isolating cells from adipose tissue is taught by Katz et al. An artisan would have also relied on the teachings of Akanbi et al. for teaching obtaining stem cells from juvenile humans and Hedrick et al. for teaching obtaining stem cells that adhere to the culture dish after an overnight culture and Djian et al. for teaching that the period allowing adherence to the dish is not more than 12 hours such that an artisan is ensured that the adherent cells have not started to divide. An artisan would have combined the

teachings these teachings with Tremain et al., who teach single-cell derived colonies, in order to arrive at lines of stem cells obtained from adipose tissue, wherein the stem cells are those that adhere to a culture dish within 12 hours of plating. With regard to Applicant referring to Exhibit E, Bernardo et al., Bernardo et al. do not teach away from adipose tissue containing stem cells. While it may be that adipose tissue does not have large amounts of stem cells as does bone marrow, Bernardo et al.'s teaching indicates that there are stem cells in adipose tissue. Further, it is noted that Katz et al. and Akanbi et al. teach that adipose tissue can be used to obtain stem cells.

Applicant indicates that the non-obvious step performed in the method of the instant invention is obtaining a cell population which originates from adipose tissue and in which the concentration of stem cells is high enough for stem cells clones to be obtrained. Tremain et al. does not address this problem because Tremain et al. does not teach stem cells from adipose tissue (Applicant's emphasis, Applicant's response, pages 3-4). In response, this is not persuasive. As discussed above, Tremain et al. was not relied upon for teaching isolation of stem cells from adipose tissue; Katz et al. and Akanbi et al. were. Tremain et al. was used to show that it is routine in the art to obtain single cell-derived colonies.

With regard to the Examiner citing Djian et al., wherein Djian et al. teach that a period of 12 hours is sufficiently long to allow adherence of cells but is too brief for appreciable replication, and the Examiner derives from this teaching that 12 hours would minimize the confusion that two cells sitting next to each other are two different cells that plat next to each other or is the result of cell division, Applicant indicates that

the relevance of this issue is not clear to Applicant. In any event, Djian et al. is relative to the cloning of adipocyte precursors and that their features are different from the cloned stem cells (Applicant's emphasis, Applicant's response, page 4). In response, this is not persuasive. With regard to Applicant indicating that the citation of Djian et al. is unclear, Djian et al. was cited to show that in order for an artisan to obtain lines of cells derived from a single cell, an artisan would have used 12 hours of plating as a cut off to ensure that every cell in the dish had not undergone replication and be ensured even if cells were next to each other in a dish, that they are not cells resulting from cell division. With regard to Applicant indicating that Djian et al. teach adipocyte precursors and are not the same stem cells as those claimed, as far as can be told, while Djian et al. give their cells a different name, the cells taught by Djian et al. are stem cells like those taught by Katz et al. and the instant specification. The only difference of the cells between the instant specification and Djian et al. is that the cells in the specification are from juvenile humans. Djian et al. processes the cells using the same method steps as those in the instant specification, adipose tissue is chopped, enzymatically digested, centrifuged, and plated for 12 hours (specification, Example 1.2 Method for Isolating Multipotent Cells from the Adipose Tissue of Young Children). Similarly, Djian et al. teach digestion of fat tissue, centrifugation, and plating for 12 hours (Djian et al., page 1201, 1st col., under Isolation of adipose precursors). As such, as far as can be told, the cells of Djian et al. are stem cells and an artisan would have combined the teaching of Akanbi et al. for obtaining stem cells from juveniles.

With regard to the citation of Young et al., Applicant indicates that it is not clear why the Examiner considers the abstract of Young et al. (or any other part of this reference) to be relevant to step e) of claim 25 as step e) of claim 25 does not recite performing bulk culture (Applicant's response, page 4). In response, the Examiner has amended the rejection, above to better address this issue.

Applicant indicates that the arguments filed on July 7, 2009 are maintained and that the assertions made by the Examiner are incorrect or not relevant (Applicant's response, page 6).

With regard to the citation of Tremain et al., Applicant indicates that the publication relates to isolation of stem cells from bone marrow. Applicant also indicates that the method disclosed by Young et al. do not teach 50 to 80 populations doublings as stated in claim 25, step e) (Applicant's emphasis, Applicant's response, page 6). In response, this is not persuasive. As indicated above, Tremain et al. was not cited as a reference used in a 102 rejection, but in a 103. Katz et al. and Akanbi et al. were cited for teaching obtaining stem cells from juvenile humans and Hedrick et al. was cited for teaching obtaining stem cells that adhere to the culture dish after an overnight culture and Djian et al. for teaching that the period allowing adherence to the dish is not more than 12 hours such that an artisan is ensured that the adherent cells have not started to divide. An artisan would have combined the teachings these teachings with Tremain et al., who teach single-cell derived colonies, in order to arrive at lines of stem cells obtained from adipose tissue, wherein the stem cells are those that adhere to a culture

dish within 12 hours of plating. With regard to the citation of Young et al., the Examiner has addressed this issue with the Young et al., US PGPublication.

Applicant indicates that adipose derive stem cells are HLA class I positive, see Gronthos et al., 2001 (Exhibit A), Katz et al., 2005 (Exhibit B), Strem et al., 2005, (Exhibit C) and Wagner et al., 2005 (Exhibit D). The cells presented in the literature are "adipose-derived stem cells" are HLA-class I positive (Applicant's emphasis, Applicant's response, page 7). In response, this is not persuasive. Applicant's referral to other publications unrelated to the rejection are not evidence that the cells obtained by the teachings of Katz et al. (WO 00/53795) and Akanbi et al. are different from those claimed. It is also noted that none of the references teach that the adipose tissue was obtained from juvenile humans. Gronthos et al. teach that the adipose tissue was obtained from adults (Gronthos et al., page 55, 2nd col., under Tissue preparation); there is no specific guidance that Katz et al., 2005, used cells from juvenile humans (Katz et al., 2005, page 414). Similarly, Strem et al., page 133, 1st col., 1st parag. teach tissue from patients whose median age was 49 and this is not specifically indicate that juvenile humans were used. Wagner et al., page 1403, 2nd col. under Mesenchymal stem cells from adipose tissue teach that adipose tissue was obtained from donors 21-40 years of age. As such, the citations of Exhibits do not overcome the rejection at hand.

Applicant indicates that Katz et al. WO/053795 provide no information relative to the HLA Class I phenotype of the cells they disclose (Applicant's emphasis, Applicant's response, page 7). In response, the combination of references is Katz et al. (WO

00/53795 in view of Akanbi et al. While none of the cited references teach the state of the HLA-class I state of the adipose-derived stem cells, the cells obtained from the combination of teachings would have been HLA-negative as Katz et al., WO 00/53795, Akanbi et al. Hedrick et al., Haynesworth et al., Tremain et al., Djian et al. Young et al., US Patent Application Publication, US 2004/0033214, Didinksy et al. provide guidance to arrive at the claimed invention. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Applicant similarly makes the same arguments as the Examiner, above, that Katz et al. WO 00/53795 teach the same methods as the references cited in the Exhibits and that Katz et al. does not teach using adipose tissue from a juvenile and that the Exhibit publications teach that the stem cells from adipose tissue are HLA Class I positive (Applicant's response, pages 7-8). The Examiner agrees with Applicant that Katz et al. WO 00/53795, alone does not teach the claimed invention. Rather, at the time of filing,

given the combination of references, an artisan would have arrived at the claimed invention.

Applicant indicates that the inventors have discovered that the MHC-I phenotype of the CA cell population obtained after steps a) to d) is positive and that it becomes negative during the course of step e). This change in phenotype is not taught in the art (Applicant's emphasis, Applicant's response, page 9). In response, "the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

With regard to the citation of Akanbi et al., Applicant indicates that the Examiner misunderstands the objective of the present invention, as the objective of the present invention is not to produce a large quantity of differentiated cells. Rather, the objective is to produce a large quantity of undifferentiated cells. Further, the objective is not either to produce a large quantity of adipose precursor cells because these cells do not have the potential to differentiate into cell types of other lineages; the objective of the instant invention is to produce large quantities of stem cells that differentiate into cells of other lineages (Applicant's emphasis, Applicant's response, pages 10-11). In response, this is not persuasive. The Examiner was not solely relying on Akanbi et al. for teaching

large quantities of adipose progenitor cells. Rather, given the combination of references, particularly, Katz et al., WO 00/53795 teach how to obtain adipose-derived stem cells and that they can be used to obtain differentiated cells of different lineages. Akanbi et al. was cited to show that at the time of filing, there was an advantage to using cells obtained from juvenile animals, particularly that they proliferated and differentiated better than cells obtained from adult animals. Given this teaching, an artisan would have been motivated to obtain stem cells from adipose tissue, as taught by Katz et al., WO 00/53795, but would have modified Katz et al.'s teaching by using juvenile humans. With regard to Applicant indicating that the objective of the instant invention is to produce a large quantity of undifferentiated cells, the combination of Katz et al. and Akanbi et al. does not preclude that an artisan cannot take the stem cells from the combination of these references and expand them to get more stem cells prior to differentiation.

Thus, the claims remain rejected.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama whose telephone number is 571-272-2911. The examiner can normally be reached Mondays, Wednesdays, Thursdays, and Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/Joanne Hama/
Primary Examiner
Art Unit 1632